Rubella

REPORT IMMEDIATELY

(Also known as German Measles)

Section 1:

ABOUT THE DISEASE

A. Etiologic Agent

Rubella is caused by the rubella virus, an enveloped, positive-stranded RNA virus (family *Togaviridae,* genus *Rubivirus*).

B. Clinical Description

When contracted after birth, rubella is usually a mild disease characterized by a generalized maculopapular rash (which sometimes begins on the face), swollen lymph nodes, and slight fever. The rash presentation can be quite variable. Up to 50% of infections occur without recognized rash. Transient inflammation of the joints rarely occurs in children but is common in adolescents and adults, especially women. Encephalitis (1 per 6,000 cases) and thrombocytopenia (1 per 3,000 cases) are rare complications.

Rubella is of greatest danger to the unborn fetus. Up to 90% of infants born to mothers infected in the first trimester will develop the physical anomalies referred to as congenital rubella syndrome (CRS). CRS is characterized by any of a number of complications and findings, including blindness, heart defects, deafness, behavioral disorders, mental retardation, growth retardation, bone disease, enlarged liver and spleen, thrombocytopenia, and purple skin lesions. Some effects may not be apparent at birth.

Reinfection has been demonstrated on rare occasions, but only very rarely has resulted in CRS.

C. Vectors and Reservoirs

Humans are the only known host for rubella.

D. Modes of Transmission

Postnatal rubella is transmitted from person to person by droplet or direct contact with the nasopharyngeal secretions of an infected person or with the nasopharyngeal secretions or urine of an infant with CRS. Transplacental infection resulting in CRS occurs in infants who are born to women with rubella occurring at 20 weeks or less of gestation.

E. Incubation Period

The incubation period is usually 16–18 days, with a range of 14–23 days.

F. Period of Communicability or Infectious Period

The infectious period is usually from seven days before to seven days after rash onset. Studies have shown presence of rubella virus in nasopharyngeal secretions ranging from 5–14 days after rash onset. However, infectiousness

decreases significantly after day five in most individuals. Rubella is similar to influenza and mumps in infectiousness and is not as contagious as measles or chickenpox.

A person who is asymptomatic but laboratory-confirmed and epidemiologically-linked to a laboratory-confirmed case that is clinically consistent with rubella should be considered infectious for 5–30 days after exposure that resulted in infection.

Infants with CRS shed virus in nasopharyngeal secretions and urine for a longer period; a small proportion continue to be infectious for one year or more.

G. Epidemiology

Rubella occurs worldwide. In temperate zones, peak incidence is in late winter and early spring. Before the widespread use of rubella vaccine, which was licensed in 1969, peaks of rubella incidence occurred in the U.S. every 6–9 years, and most cases occurred in children. Most reported rubella in the U.S. since the mid-1990's has occurred among Hispanic young adults who were born in areas where rubella vaccine is not routinely given and who were never exposed to rubella in their countries of origin. The percentage of susceptible people may be higher in certain immigrant population groups, especially adolescent and adult males from Latin America.

Most adults born in the U.S. before 1957 have been infected naturally and are probably immune to rubella. Recent serologic surveys indicate that about 10% of young adults are susceptible to rubella. In recent years in the U.S. and in Massachusetts, outbreaks have occurred among immigrant populations due to lack of rubella vaccination programs in their countries of origin. Outbreaks now occur predominantly in workplaces and communities at large, although school settings have been affected.

CRS now disproportionately affects infants born to foreign-born women. Identifying and managing susceptible pregnant women who may have been exposed to rubella is particularly challenging, especially in community-wide outbreaks.

H. Bioterrorist Potential

This pathogen is not considered to be of risk for use in bioterrorism.

Section 2:
REPORTING CRITERIA AND LABORATORY TESTING

A. What to Report to the Massachusetts Department of Public Health (MDPH)

Report any of the following:

- A case of rash illness accompanied by fever;
- A suspect case of rubella (with or without fever), as diagnosed by a health care provider;
- Positive serologic test for immunoglobulin M (IgM) antibody against rubella virus;
- Significant rise between acute- and convalescent-phase titers in serum rubella immunoglobulin G (IgG) antibody or total antibody level by any standard serologic assay;
- Isolation of rubella virus from a clinical specimen; or

- A suspect or confirmed case of CRS in a child (usually a baby), as diagnosed by a health care provider (the CRS case definition appears under the *Additional Information* section at the end of this chapter).

Note: See Section 3C for information on how to report a case.

B. Laboratory Testing Services Available

Note: Please refer to Attachment A: Memorandum on Diagnosis of Rubella Infection in Pregnant Women Exposed to Rubella and in Their Babies (found at the end of this chapter) for details about diagnostic testing for CRS.

Serologic Tests in Non-Congenital Rubella

Rubella IgM Test

It is very important to obtain laboratory confirmation of cases of rubella and suspect cases of rubella. Due to cross-reacting antibodies and other test issues, there are problems related to the sensitivity and specificity of commercially available IgM tests. The specimen should be drawn at least three days after onset of rash (to minimize the possibility of false negative results) and within six weeks of rash onset. (If serum is collected prior to the third day, a follow-up specimen may be requested.) This test is performed at the MDPH State Laboratory Institute (SLI), and the amount of serum required is 2 mL.

Rubella Total Antibody Paired-Titer Test

Paired total antibody testing can be helpful when rubella IgM results are not interpretable. Acute serum should be collected as soon as possible after rash onset; convalescent serum should be collected 14 days later. Paired testing for rubella is performed at the SLI only under special circumstances and after consultation with a MDPH immunization epidemiologist at (617) 983-6800 or (888) 658-2850. The amount of serum required is 2 mL.

Shipment of Sera

Please refer to *Attachment B: Instructions for Collection of Serologic Specimens from Suspect Cases (Including CRS Infants)* (found at the end of this chapter) for instructions on collecting and submitting specimens to the SLI. Sera should be sent on a cold pack, with a completed SLI *Specimen Submission Form* (found at the end of this chapter and on the MDPH website at www.mass.gov/dph/bls/generalform.pdf) to:

Virus Serology Laboratory
Massachusetts Department of Public Health, State Laboratory Institute (SLI)
305 South Street
Jamaica Plain, MA 02130

Before sending sera, please call a MDPH immunization epidemiologist at (617) 983-6800 or (888) 658-2850.

Virus Isolation/Molecular Characterization of Rubella

Virus isolation is much less useful for disease control purposes than serologic testing because results are not available for several weeks. However, molecular characterization of isolated rubella virus is an extremely important tool in epidemiologic research to determine, for example, the source of the infection and which cases and outbreaks

are linked to each other. Also, in cases where serology is not useful or possible—for example, when a suspect case has been recently vaccinated with the measles, mumps, and rubella (MMR) vaccine—virus isolation can be used for confirmation, and molecular characterization can distinguish wild-type virus from vaccine virus. Specimens for rubella virus isolation should be submitted, along with the SLI *Specimen Submission Form* (found at the end of this chapter or on the MDPH website at www.mass.gov/dph/bls/generalform.pdf), to the SLI Virus Isolation Laboratory, which will forward them to the Centers for Disease Control and Prevention (CDC). Please contact a MDPH immunization epidemiologist at (617) 983-6800 or (888) 658-2850 about submitting specimens for virus isolation, and consult *Attachment B: Instructions for Collection of Serologic Specimens from Suspect Cases (Including CRS Infants)* at the end of this chapter.

Polymerase Chain Reaction (PCR)

PCR can be used to detect the presence of rubella virus in tissue culture or directly in clinical specimens. It can also be used for molecular characterization. Specimens submitted to the SLI Virus Isolation Laboratory for rubella virus PCR and characterization will be forwarded to the CDC.

Remember to use the SLI *Specimen Submission Form*, found at the end of this chapter or on the MDPH website at www.mass.gov/dph/bls/generalform.pdf, when submitting any clinical specimens to the SLI.

Section 3:

REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To identify cases and susceptible exposed people, and to prevent further spread of infection, especially to pregnant women.
- To ensure appropriate management of exposed pregnant women and their babies.
- To monitor the effectiveness of outbreak control strategies.
- To identify cases of congenital rubella infection/syndrome that may occur after a cluster or outbreak of rubella.
- To identify the source of infection by virus isolation and molecular characterization.
- To identify virus strains circulating in the U.S., and to determine whether they are endemic.

B. Laboratory and Health Care Provider Reporting Requirements

Rubella is reportable to the local board of health (LBOH). The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of rubella, as defined by the reporting criteria in Section 2A.

Due to the health implications of rubella, the MDPH requests that information about any case of rubella also be immediately reported to a MDPH immunization epidemiologist at the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of rubella infection shall immediately report such evidence of infection, directly by phone, to the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

C. Local Board of Health (LBOH) Reporting and Follow-Up Responsibilities

Reporting Requirements

MDPH regulations *(105 CMR 300.000)* stipulate that rubella is reportable to the LBOH and that each LBOH must report any case of rubella or suspect case of rubella, as defined by the reporting criteria in Section 2A. Cases should be reported to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS) using a MDPH *Rubella Case Report Form* (found at the end of this chapter). Refer to the *Local Board of Health Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

Due to the health implications of rubella, the MDPH requests that information about any suspect or known case of rubella (as defined by the criteria in Section 2A) be immediately reported to the MDPH Division of Epidemiology and Immunization by calling (617) 983-6800 or (888) 658-2850.

Case Investigation

Due to national surveillance and reporting requirements, the Massachusetts Immunization Program (MIP) will take the lead on rubella and CRS case investigation (including filling out the case report form and reporting it to ISIS) and disease control recommendations, in collaboration with the LBOH. The MIP will keep the LBOH informed of all significant developments and will request the assistance of the LBOH as needed.

In order to assess the likelihood that a suspect case is a true case prior to laboratory testing, the MDPH and/or other public health staff involved in the investigation should ask about:

1. Clinical presentation;
2. Rubella immunization history;
3. Country of origin and length of residence in U.S. (those in the U.S. for a short time are more likely to be susceptible);
4. Recent history of travel (to where and dates);
5. Whether there were any recent out-of-town visitors (from where and dates);
6. Whether there was any recent contact with anyone with similar symptoms;
7. Exposure and transmission settings (e.g., childcare, school, health care setting, prisons, and work settings where the foreign-born are employed);
8. Risk factors for disease (e.g., <12 months of age, pregnant, or immunosuppressed);
9. Pregnancy status if the suspect case is a woman of childbearing age (12–50 years of age); and
10. Laboratory information, including viral isolation and serologic test results.

Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.

Section 4: CONTROLLING FURTHER SPREAD

This section provides detailed control guidelines that are an integral part of case investigation. LBOH should familiarize themselves with the information. However, the MDPH will take the lead on implementing control measures, in collaboration with the LBOH.

A. Isolation and Quarantine Requirements *(105 CMR 300.200)*

Non-Congenital Rubella

Minimum Period of Isolation of Patient

Until seven days after onset of rash (counting the day of rash onset as day zero).

Minimum Period of Quarantine of Contact

Students and staff born in or after 1957 who are not appropriately immunized or who do not have laboratory evidence of immunity will be excluded from work or classes from the 7th through the 21st day after their last exposure. When multiple cases occur, susceptibles need to be excluded until 21 days after the onset of the last case at the school or workplace. Health care workers (or patients) who are not appropriately immunized or do not have laboratory evidence of immunity will be excluded from work (or isolated) from the 7th through the 21st day after their last exposure. Susceptible health care workers who are vaccinated post-exposure should be excluded through the 23rd day after their last exposure. In certain outbreak situations deemed to be high-risk, the MDPH may recommend additional control measures.

Congenital Rubella

Minimum Period of Isolation of Patient

Isolation from susceptible persons for the first year of life or until two viral cultures of clinical specimens (nasopharyngeal secretions or urine), obtained one month apart after age three months, are negative for rubella virus.

Minimum Period of Quarantine of Contacts

No restrictions except for susceptibles. Same as for non-congenital rubella, above.

B. Protection of Contacts of a Case (Immunization, Prophylaxis, or Other Measures)

Note: Control measures for CRS can be found in Section 4C.

1. Implement control measures before serologic confirmation.
2. Inquire about contact with a known or suspect case of rubella and travel during the rubella exposure period (14–23 days prior to rash onset). Ask other questions listed in Section 3C.
3. Isolate the case during his/her infectious period (until seven days after rash onset).

4. Identify all those exposed. Think in terms of the "zones of exposure" and consider members of the following groups, if they were in contact with the case during his/her infectious period:
   a. Household members,
   b. School/daycare contacts (students and staff),
   c. Staff and patients at medical facility where patient was seen,
   d. Individuals at workplace of case (especially daycare centers, schools, and medical settings),
   e. Members of same religious/social groups,
   f. Members of sports teams and other extracurricular groups,
   g. Bus or carpool mates,
   h. Close friends, and
   i. Persons potentially exposed at social events, travel sites, etc.
5. Identify high-risk susceptibles, including women of childbearing age (12–50 years of age), with whom the case had contact during his/her infectious period. Pregnant women are particularly important to identify because of the risk of CRS. Pregnant women, infants <12 months of age, and immunocompromised individuals should be referred to their obstetricians/health care providers. A line-listing of pregnant contacts must be developed.
6. Identify all other susceptibles; that is, individuals without proof of immunity as defined below:

Proof of Immunity to Rubella[1]

- Birth in the U.S. before 1957, unless a woman of child-bearing age who is pregnant or could become pregnant, a health care worker, or a college student;
- Documentation of rubella vaccination on or after the first birthday, unless a pregnant woman;[2] or
- Serologic proof of immunity.

1 Persons born outside the U.S. (without written proof of immunity) are considered susceptible, regardless of year of birth.
2 Serologic evidence of immunity is the only acceptable proof of immunity for pregnant women.

7. Immunize all susceptibles. Live-virus rubella vaccine given after exposure has not been demonstrated to prevent illness, but theoretically, could prevent illness if administered within three days of exposure. All susceptibles who are ≥12 months of age (and for whom it is not contraindicated) should receive rubella vaccine given as the combined formulation of MMR vaccine. Please review *Attachment C: Measles, Mumps, Rubella (MMR) Vaccine Fact Sheet* at the end of this chapter.
8. Isolation/exclusion (non-health care settings):
   a. Case: Isolate and exclude the symptomatic cases during the infectious period (from seven days before until seven days after rash onset, counting the day of rash onset as day zero). He/she may return to normal activities on the eighth day. Confirmed asymptomatic cases should be isolated/excluded on days 5–30 after the last day of exposure to the case that was the origin of the infection.
   b. Contacts: Exclude exposed susceptible individuals as follows:
      i. If there was a discrete (one-time) exposure, exclude from days 7–21 from that exposure.
      ii. If there was continuous exposure, exclude from days 7–21 from the day of rash onset in the case.

iii. If there is more than 1 case of rubella, exclude until 21 days after the onset of rash in the last reported case in the outbreak setting.

iv. If exposed susceptible contacts are vaccinated, they may return to work, school, etc.

9. Conduct surveillance for 2 incubation periods (42 days) after rash onset in the last case or the last exposure in the setting, whichever is later.

C. Managing Special Situations

Control guidelines for three situations are presented below: 1) rubella in health care facilities; 2) exposure of a pregnant woman to rubella; and 3) infants with CRS. Please note that these situations are not mutually exclusive.

Situation 1: Rubella in Health Care Facilities

If a confirmed or suspect case of rubella has visited a health care facility during his/her infectious period, contact the infection control staff and go over the following recommendations with them:

1. Identify all high-risk patients and staff exposed to the rubella case. It is especially important to identify women of childbearing age (12–50 years of age). Pregnant women and immunosuppressed individuals should be referred to their health care providers to determine if they are immune.

   Pregnancy and Immune Globulin (IG): Routine use of IG for post-exposure prophylaxis is not recommended, even for susceptible pregnant women, because IG does not guarantee prevention of fetal infection. The only time IG may be considered is when infection occurs early in pregnancy and termination is not an option.

2. Identify all other susceptible exposed patients and staff at the facility. Pediatricians of exposed infants should be notified. Proof of immunity is defined as:

Proof of Immunity to Rubella[1]

- Birth in the U.S. before 1957, unless a woman of child-bearing age who is pregnant or could become pregnant, a health care worker, or a college student;
- Documentation of rubella vaccination on or after the first birthday, unless a pregnant woman;[2] or
- Serologic proof of immunity.

1 Persons born outside the U.S. (without written proof of immunity) are considered susceptible, regardless of year of birth.

2 Serologic evidence of immunity is the only acceptable proof of immunity for pregnant women.

3. Notify health care providers of all exposed patients.

4. Immunize all susceptible patients and staff. Live-virus rubella vaccine given after exposure has not been demonstrated to prevent illness but theoretically could prevent illness if administered within three days of exposure. All susceptibles who are ≥12 months of age (and for whom it is not contraindicated) should receive rubella vaccine given as the combined formulation of MMR vaccine. Please review *Attachment C: Measles, Mumps, Rubella (MMR) Vaccine Fact Sheet* at the end of this chapter.

Previous administration of human anti-Rho(D) immune globulin (RhoGam) does not generally interfere with an immune response to rubella vaccine. However, women who have received anti-Rho immune globulin should be tested serologically 6–8 weeks after vaccination to assure that seroconversion occurred. If other antibody-containing blood products are needed for other reasons, they should be administered at least 2 weeks before and deferred for up to 11 months after administration of MMR vaccine.

5. Exclude susceptible staff. Unlike measles, vaccinating immediately post-exposure has not been documented to prevent an individual from acquiring rubella. Therefore, all susceptible individuals without proof of immunity can become infectious and must be excluded on days 7–21 post-exposure. They may return on the 22nd day. Those who are vaccinated should be excluded on days 7–23 post-exposure and may return on the 24th day. Those who are unvaccinated must be excluded on days 7–21 and may return on the 22nd day. If additional cases occur, the exclusion period may need to be extended.

6. Isolate susceptible patients and suspect/confirmed cases:

    a. Case: All suspect and confirmed cases should be placed on standard and droplet precautions during their infectious period. The infectious period for rubella is seven days before through seven days after rash onset. They may be taken off precautions on the eighth day. Isolate and exclude the symptomatic cases during the infectious period (from seven days before until seven days after rash onset, counting the day of rash onset as day zero). He/she may return to normal activities on the eighth day. Confirmed asymptomatic cases should be isolated/excluded on days 5–30 after the last day of exposure.

    b. Contacts: Susceptible patients ≥12 months of age should be vaccinated and placed on standard and droplet precautions for days 7–21 after exposure. Those who are unvaccinated must be excluded on days 7–21 post-exposure and may return on the 22nd day. They may be taken off precautions on the 22nd day. Those who are vaccinated should be excluded 7–23 days post-exposure and may return on the 24th day.

7. Conduct surveillance for 2 incubation periods (42 days) after the last exposure in the facility, and report all suspect cases of rubella to the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

8. Place any new cases of rash illness on standard and droplet precautions or exclude as described in #6 above. A serum specimen should be obtained three days after rash onset and sent to the SLI. New cases should be reported to the MDPH immediately.

Situation 2: Exposure of a Pregnant Woman to Rubella

1. Obtain additional information regarding:
    a. Number of weeks of gestation at exposure;
    b. Previous evidence or date of immunity;
    c. Previously diagnosed rubella infection and date;
    d. Date and specific titer result of previous serum rubella immunoglobulin G (IgG) titer; and
    e. Pregnancy outcome, when available.

2. Contact the prenatal-care provider, and determine the exposed pregnant woman's immune status. Send the provider the memo in *Attachment A: Diagnosis of Rubella Infection in Pregnant Women Exposed to Rubella and in Their Babies* (at the end of this chapter). Immunity must be documented by a verified, dated record of

a positive serologic test; documentation of having received rubella-containing vaccine does not constitute proof of immunity for exposed pregnant women. Nevertheless, it is important to collect such documentation of prior rubella vaccination because it serves to reduce the level of suspicion (and anxiety) about rubella infection; it aids in the interpretation of the laboratory results; and it allows identification of reinfection.

3. If the woman is susceptible, arrange for diagnostic testing. Serial serologic tests for rubella in the susceptible pregnant woman (i.e., one without a pre-existing positive serology test) are described in *Attachment A: Diagnosis of Rubella Infection in Pregnant Women Exposed to Rubella and in Their Babies.* To determine whether or not infection occurred may require as many as three blood specimens collected within a six-week period. If the outbreak (and potential for exposure) continues beyond this initial six-week testing period, specimens should be collected from susceptible exposed pregnant women every 10–14 days if exposure continues, or every 3–4 weeks in cases of no defined exposure, and tested together with the first specimen. Diagnostic testing of susceptible pregnant women will be necessary in all cases of presumed or possible exposure:

   a. Regardless of the point in pregnancy in which the exposure occurred (because of the possibility of late effects), and

   b. Regardless of whether the woman had symptoms of rubella (because of the high proportion of asymptomatic infections).

   Diagnostic testing of the baby, also described in *Attachment A: Diagnosis of Rubella Infection in Pregnant Women Exposed to Rubella and in Their Babies*, will be necessary if rubella infection in the mother was not reliably ruled out, as reflected below:

Pregnant Woman's Laboratory Results

	Rubella IgM-negative and no rise in IgG	Rubella IgM-positive or significant rise in IgG	Maternal infection neither confirmed nor ruled out prior to delivery
Woman infected?	No	Yes	Unknown
Need to follow baby?	No	Yes—See *Attachment A*	Yes—See *Attachment A*

Situation 3: Infants with CRS

In cases of suspect or confirmed CRS in an infant, contact the infection control staff in any facility in which the infant was seen, as well as the obstetrician and the pediatrician (if any); fax them the memorandum in *Attachment A: Diagnosis of Rubella Infection in Pregnant Women Exposed to Rubella and in Their Babies* (at the end of this chapter), and review these recommendations with them:

1. Immediately place all suspect cases of CRS on contact precautions. Infants with CRS shed virus in their urine and nasopharyngeal secretions and can remain infectious for one year or more after birth. Both the American Academy of Pediatrics (AAP), in the *Red Book*, and the CDC, in the *CDC Guidelines for Isolation and Precautions in Hospitals,* recommend contact precautions.

2. Place all suspect and confirmed cases of rubella on droplet precautions during their infectious period. The infectious period for rubella is from seven days before until seven days after rash onset. Confirmed asymptomatic cases should be isolated/excluded on days 5–30 after the last day of exposure.

3. Identify all high-risk patients and staff exposed to the CRS and/or rubella case(s). It is especially important to identify women of childbearing age (12–50 years of age). Pregnant women and immunosuppressed individuals should be referred to their health care providers to determine if they are immune.

   Pregnancy and Immune Globulin (IG): Routine use of IG for post-exposure prophylaxis is not recommended, even for susceptible pregnant women, because IG does not prevent infection or viremia in the mother and does not guarantee prevention of fetal infection. In addition, it might modify or suppress symptoms and create an unwarranted sense of security. Therefore, the only time IG may be considered is when infection occurs early in pregnancy and termination is not an option. In such cases, 20 mL of IG given intramuscularly within 72 hours of exposure, might reduce—but not eliminate—the risk of rubella.*

4. Identify all other susceptible exposed patients and staff at the facility. Pediatricians of exposed infants should be notified. If a baby with CRS has been in a nursery where visitors and other family members have spent significant amounts of time, the immunity of those exposed to the baby should be evaluated. Proof of immunity includes:

Proof of Immunity to Rubella[1]

- Birth in the U.S. before 1957, unless a woman of child-bearing age who is pregnant or could become pregnant, a health care worker, or a college student;
- Documentation of rubella vaccination on or after the first birthday, unless a pregnant woman;[2] or
- Serologic proof of immunity.

1 Persons born outside the U.S. (without documented proof of immunity) are considered susceptible, regardless of year of birth.

2 Serologic evidence of immunity is the only acceptable proof of immunity for pregnant women.

5. Notify health care providers of all exposed patients.

6. Immunize all susceptible patients and staff. Live-virus rubella vaccine given after exposure has not been demonstrated to prevent illness, but theoretically could prevent illness if administered within three days of exposure. All susceptibles who are ≥12 months of age (and for whom it is not otherwise contraindicated) should receive rubella vaccine given as the combined formulation of MMR vaccine. Please review *Attachment C: Measles, Mumps, Rubella (MMR) Vaccine Fact Sheet* at the end of this chapter.

   Previous administration of human anti-Rho(D) immune globulin (RhoGam) does not generally interfere with an immune response to rubella vaccine. However, women who have received anti-Rho immune globulin should be serologically tested 6–8 weeks after vaccination to assure that seroconversion occurred. If other antibody-containing blood products are needed for other reasons, they should be administered at least 2 weeks before and deferred for up to 11 months after administration of MMR vaccine.

7. Exclude susceptible staff. Unlike measles, vaccinating immediately post-exposure has not been documented to prevent an individual from acquiring rubella. Therefore, all susceptible individuals without proof of immunity can become infectious and must be excluded on days 7–21 post-exposure. They may return on the 22nd day. Those who are vaccinated must be excluded on day 7–23 and may return the 24th day. If additional cases occur, the exclusion period may need to be extended.

* Limited data indicate that IG in a dose of 0.55 mL/kg may prevent or modify infection in an exposed, susceptible person. In one study, the attack rate of clinically apparent infection was reduced from 87% in control subjects to 18% in recipients of IG. However, the absence of clinical signs in a woman who has received IG does not guarantee that fetal infection has been prevented. In this study, 44% of the IG recipients were infected. Infants with congenital rubella are known to have been born to mothers who were given IG shortly after exposure.

8. Isolate susceptible patients and suspect/confirmed cases. Susceptible patients ≥12 months of age should be vaccinated and placed on droplet precautions for days 7–21 after exposure. They may be taken off precautions on the 22nd day. Those who are vaccinated should be excluded 7–23 days post-exposure and may return on the 24th day. All suspect and confirmed cases should be placed on droplet precautions during their infectious period. The infectious period for rubella is seven days before until seven days after rash onset. They may be taken off precautions on the eighth day. Confirmed asymptomatic cases should be isolated/excluded on days 5–30 after the last day of exposure.
9. Collect specimens for diagnostic testing on infants with suspect CRS and their mothers, as detailed in *Attachment A: Diagnosis of Rubella Infection in Pregnant Women Exposed to Rubella and in Their Babies* (found at the end of this chapter).
10. Conduct surveillance for 2 incubation periods (46 days) after the last exposure in the facility, and report all suspect cases of rubella to the MIP at (617) 983-6800 or (888) 658-2850.
11. Take the opportunity to review the facility's policy on post-partum immunization of susceptible women. The MIP provides MMR vaccine to all maternity services for routine vaccination of post-partum susceptible patients as well as for outbreak control. Birthing facilities should be informed of this and encouraged to adopt a policy of routine post-partum vaccination.

D. Preventive Measures

Although good personal hygiene (which consists of proper handwashing, disposal of used tissues, not sharing eating utensils, etc.) is important in preventing rubella, vaccination, including routine childhood vaccination, catch-up vaccination of adolescents, and targeted vaccination of high-risk adult groups (such as international travelers and adults born outside the U.S.), is the best preventive measure. Health care and other workers born outside the U.S. are a potentially susceptible population in which outbreaks may occur after importation of the virus from areas where rubella is endemic. Vaccinating against rubella in workplaces is a strategy to reach this susceptible population and can be a critical step in eliminating indigenous rubella.

The continuing occurrence of rubella among women of childbearing age indicates the need to continue vaccination of susceptible women in this age group. The absence of evidence of vaccine teratogenicity suggests that the practice is safe. Vaccination of susceptible women of childbearing age should:

- Be part of routine general medical and gynecological outpatient care;
- Take place in all family-planning settings; and
- Be provided routinely before discharge from any hospital, birthing center, or other medical facility, unless a specific contraindication exists. *(Note: Previous administration of human anti-Rho(D) immune globulin [RhoGam] does not generally interfere with an immune response to rubella vaccine. However, women who have received anti-Rho immune globulin should be serologically tested 6-8 weeks after vaccination to ensure that seroconversion occurred.)*

Reasonable practices in any immunization program include:

- Asking women if they are pregnant;
- Not vaccinating pregnant women;
- Explaining the potential risk for the fetus to women who state that they are not pregnant; and

- Counseling women who are vaccinated not to become pregnant during the three months following MMR vaccination.

Recommend that pregnant women with an unknown immune status restrict activities to avoid exposure while waiting for serologic test results. During this time, pregnant women should be excluded from activities (e.g., work or school) that present the possibility of exposure to persons with confirmed or suspect cases of rubella. Pregnant women found to be susceptible to rubella should avoid these settings for six weeks (two incubation periods) after the onset of symptoms of rubella in the last patient for whom rubella cannot be ruled out.

During outbreaks, susceptible pregnant women should be advised to avoid the affected setting(s) (e.g., schools, military settings, workplace, churches, athletic events, or other social gatherings).

Remember to evaluate all adults, especially women of child-bearing age, for needed immunizations at every encounter with the health care system. All foreign-born adults without vaccination records should be vaccinated with MMR.

The MDPH will provide detailed rubella infection control recommendations. Please call a MDPH immunization epidemiologist at (617) 983-6800 or (888) 658-2850.

Please refer to the most current versions of the Advisory Committee on Immunization Practices (ACIP) statement on measles, rubella, and mumps (listed in the *References* section), MDPH's *Immunization Guidelines,* and MDPH's *Massachusetts Immunization Program State-Supplied Vaccines and Patient Eligibility Criteria* for details about MMR vaccine, the recommended schedule, who should and shouldn't get the vaccine, and who is eligible to receive state-supplied vaccine. These, as well as other relevant resources, are available through the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850, and on the MDPH website at www.mass.gov/dph/cdc/epii/imm/imm.htm#mso.

A Rubella Public Health Fact Sheet for the general public can be obtained from the MDPH Division of Epidemiology and Immunization or on the MDPH website at www.mass.gov/dph. Click on the "Publications and Statistics" link, and select the "Public Health Fact Sheets" section under "Communicable Disease Control."

ADDITIONAL INFORMATION

The following are formal CDC surveillance case definitions for rubella and CRS. It is provided for your information only and should not affect the investigation and reporting of a case that fulfills the criteria in Section 2A of this chapter. (The CDC and the MDPH use the CDC case definitions to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2A.

Note: The most up-to-date CDC case definitions are available on the CDC website at www.cdc.gov/epo/dphsi/casedef/case_definitions.htm.

Case Definition for Rubella

Clinical Case Definition

An illness that has all the following characteristics:

- Acute onset of generalized maculopapular rash;
- Temperature >99.0°F (>37.2°C), if measured; and
- Arthralgia/arthritis, lymphadenopathy (usually suboccipital, postauricular, and cervical), or conjunctivitis.

Laboratory Criteria for Diagnosis

- Isolation of rubella virus;
- Detection of virus by reverse transcriptase polymerase chain reaction (RT-PCR);
- Significant rise between acute- and convalescent-phase titers in serum rubella immunoglobulin G (IgG) antibody level by any standard serologic assay; or
- Positive serologic test for rubella immunoglobulin M (IgM) antibody.

Case Classification

Suspect	Any generalized rash illness of acute onset.
Probable	A case that meets the clinical case definition, has no or noncontributory serologic or virologic testing, and is not epidemiologically-linked to a laboratory-confirmed case.
Confirmed	A case that is laboratory-confirmed or that meets the clinical case definition and is epidemiologically-linked to a laboratory-confirmed case.
Asymptomatic Confirmed	A laboratory-confirmed case in a person who is asymptomatic that is also epidemiologically-linked to a laboratory-confirmed case clinically consistent with rubella.

Case Definition for Congenital Rubella Syndrome (CRS) (as defined by CSTE, 1999)

Clinical Case Definition

CRS resulting from rubella infection in-utero usually manifests in infancy and is characterized by clinical signs or symptoms from the following categories:

1. Cataracts/congenital glaucoma, congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis), loss of hearing, and pigmentary retinopathy.
2. Purpura, hepatosplenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis, and radiolucent bone disease.

Clinical Description

Presence of any defect(s) or laboratory data consistent with congenital rubella infection. Infants with CRS usually present with more than one sign or symptom consistent with congenital rubella infection. However, infants may present with a single defect. Deafness is the most common single defect.

Laboratory Criteria for Diagnosis

- Isolation of rubella virus;
- Detection of virus by reverse transcriptase polymerase chain reaction (RT-PCR);
- Demonstration of rubella-specific immunoglobulin M (IgM) antibody; or
- Infant rubella antibody level that persists at a higher level and for a longer period than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a two-fold dilution per month).

Case Classification

Suspect	A case with some compatible clinical findings but not meeting the criteria for a probable case.
Probable	A case that is not laboratory-confirmed and that has any two complications listed in bullet (1) of the clinical case definition or one complication from bullet (1) and one from bullet (2), and lacks evidence of any other etiology.
Confirmed	A clinically consistent case that is laboratory-confirmed.
Infection Only	A case that demonstrates laboratory evidence of infection, but without any clinical symptoms or signs.

Comment

In probable cases, either or both of the eye-related findings (cataracts and congenital glaucoma) count as a single complication. In cases classified as infection only, if any compatible signs or symptoms (e.g., hearing loss) are identified later, the case is reclassified as confirmed.

Please refer to *Measles, Mumps, and Rubella—Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome and Control of Mumps: Recommendations of the Advisory Committee on Immunization Practices (ACIP)* (listed under *References* section), the most current versions of MDPH's *Immunization Guidelines,* MDPH's model standing orders for measles, mumps and rubella (MMR) vaccine, and *Massachusetts Immunization Program State-Supplied Vaccines and Patient Eligibility Criteria* for recommended schedules, groups recommended, and groups eligible to receive state-supplied vaccine.

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ATTACHMENTS

Attachment A: Memorandum on Diagnosis of Rubella Infection in Pregnant Women Exposed to Rubella and in Their Babies

Attachment B: Instructions for Collection of Serologic Specimens from Suspect Cases (Including CRS Infants)

Attachment C: Measles, Mumps, Rubella (MMR) Vaccine Fact Sheet

Attachment A

Memorandum on Diagnosis of Rubella Infection in Pregnant Women Exposed to Rubella and in Their Babies

[See next page]

Updated 9/2005

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
State Laboratory Institute
305 South Street, Jamaica Plain, MA 02130

BUREAU OF COMMUNICABLE DISEASE CONTROL

MITT ROMNEY
GOVERNOR

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LIEUTENANT GOVERNOR

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SECRETARY

PAUL J. COTE, JR.
COMMISSIONER

M E M O R A N D U M

To: Obstetricians, gynecologists, nurse midwives, nurse practitioners, nurses

From: _____, Epidemiologist
Massachusetts Immunization Program (MIP)
Massachusetts Department of Public Health (MDPH)

Date: _____

Subj.: Diagnosis of rubella infection in pregnant women exposed to rubella and in their babies

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Congenital rubella syndrome (CRS) occurs in up to 90% of infants born to women who are infected with the rubella virus during the first trimester of pregnancy. When maternal infection occurs in the first half of pregnancy, 20–25% of fetuses will be born with CRS. The most common congenital defects are cataracts, heart defects, sensorineural deafness, and developmental delay. Other problems include glaucoma, pigmentary retinopathy, microcephaly, meningoencephalitis, radiolucent bone defects, and liver or spleen involvement.

Although the risk of congenital defects decreases after the first trimester, CRS can also occur with second trimester infection. Sensorineural deafness is the single most common defect associated with CRS and has been noted even when infection occurs beyond 20 weeks gestation.

Although thought to be rare, instances of fetal infection and CRS caused by maternal reinfection during pregnancy have been documented, including one such occurrence in Massachusetts in 1994. Thus, preexisting evidence of rubella immunity, while reassuring, cannot be taken as a guarantee that an exposed pregnant woman and her fetus will be protected from infection.

Infected babies who appear normal at birth should be followed closely during the first few years of life, as congenital rubella-related defects such as deafness and cognitive/developmental problems may appear later. Universal newborn hearing screening programs help detect CRS. Because hearing impairment is the most common single defect associated with CRS, newborns who fail hearing screening tests should be tested for rubella-specific immunoglobulin M (IgM) antibodies to rule out CRS. The Massachusetts Department of Public Health (MDPH) does this serologic testing. In addition, these normal-appearing infants may still be infectious.

The MDPH provides the following recommendations regarding management of pregnant women exposed to rubella and their babies. These recommendations largely concern issues of diagnosis, which can be difficult given that rash is present in only about half of cases.

1. Rubella Exposure and Infection in Pregnant Women and Those Who Have Recently Delivered

Pregnant Woman Exposed to Rubella, Regardless of Symptoms

- Verify number of weeks of gestation at time of exposure, dates of rubella immunization, and dates and results of serologic tests. Note that documentation of rubella immunization does not constitute proof of immunity for exposed pregnant women; immunity must be documented by a verified, dated record of a positive serology test. Nevertheless, it is important to collect documentation of prior rubella vaccination, because it serves to reduce the level of suspicion (and anxiety) about rubella and aids in the interpretation of the laboratory test results.
- If a woman is susceptible (i.e., without pre-existing serologic evidence of immunity), draw blood specimens for rubella IgM and IgG serologic testing according to the following schedule:
  - 1st: As soon as possible after exposure; freeze an aliquot for possible repeat testing.
  - 2nd: At 2–3 weeks after 1st; to be tested concurrently with 1st.
  - 3rd: At 6 weeks after 1st; to be tested concurrently with 1st.
- If the outbreak (and potential for exposure) continues beyond this initial 6-week testing period, specimens should be collected from susceptible exposed pregnant women every 10–14 days if exposure continues or every 3–4 weeks in situations of no exposure, and tested together with the first specimen.
- If a rash or rubella-like symptoms develop, even in a woman with pre-existing serologic evidence of immunity, collect a blood specimen at ≥3 days after rash onset.
- Send each specimen to the MDPH State Laboratory Institute (SLI)—see attached protocol and submission form.
- Interpret serologic results as follows:
  - If either rubella IgM or a significant (≥four-fold) rise in rubella IgG titer is detected, the woman has been infected—no further serologic testing of the mother is necessary. Try to determine the timing of infection, if possible.
  - If all the above serologic tests are negative for rubella IgM and there is no significant rise in rubella IgG titer, the woman may be assumed to have avoided infection. However, bear in mind that if the first blood was not collected until several weeks after exposure, it may not be possible to detect an infection resulting from that exposure, as rubella IgM only stays elevated for about six weeks.
- If rubella infection in the mother was not reliably ruled out, follow and document the pregnancy outcome (e.g., termination, CRS, normal infant). The MIP will be contacting you to collect this information. Diagnostic testing of the baby will be necessary, as reflected below:

Pregnant Woman's Laboratory Results

	Rubella IgM-negative and no rise in IgG	Rubella IgM-positive or significant rise in IgG	Maternal infection neither confirmed nor ruled out prior to delivery
Woman infected?	No	Yes	Unknown
Need to follow baby?	No	Yes—See Section 2	Yes—See Section 2

- Recommend restricting activities to avoid exposure while waiting for serologic test results. During this time, pregnant women should be excluded from activities (e.g., work or school) that present the possibility of exposure to persons with confirmed or suspect cases of rubella. Pregnant women found to be susceptible to rubella should avoid these settings for six weeks (two incubation periods) after the onset of symptoms of rubella in the last patient for whom rubella cannot be ruled out.

Immune Globulin (IG)

The use of IG for post-exposure prophylaxis of rubella in early pregnancy does not prevent infection or viremia in the mother and does not guarantee prevention of fetal infection, and therefore, it is not routinely recommended.* In addition, it might modify or suppress symptoms and create an unwarranted sense of security. Administration of IG should be considered only if termination of the pregnancy is not an option. In such cases, 20 mL of IG given intramuscularly within 72 hours of exposure, might reduce—but not eliminate—the risk of rubella.*

Woman Possibly Exposed to Rubella During Pregnancy but Not Tested Before Delivery

Regardless of whether symptoms were present, collect acute and convalescent sera for rubella IgM and IgG testing and send to the SLI (see *Attachment B: Instructions for Collection of Serologic Specimens from Suspect Cases [Including CRS Infants]*). If the acute specimen is positive for rubella IgM, this indicates that infection occurred and no further testing of the mother is necessary.

2. Diagnosis of Rubella in Infants Born to Women with Confirmed or Suspect Rubella Infection

- Regardless of the point in pregnancy at which infection is believed to have occurred, obtain laboratory confirmation (or rule-out) of fetal infection as follows:
  - Collect specimens for virus isolation according to the attached protocol; 100% of congenitally infected newborns excrete rubella virus in nasopharyngeal secretions and urine at birth. Virus may be shed from the throat and urine for a year or longer. Specimens for virus isolation should be obtained at birth, age 3 months, and then every 1–2 months until 2 consecutive cultures are negative, at which point the baby can be assumed to no longer be infectious. This test is useful both for determining whether the infant is infectious as well as for diagnosing fetal infection—culture is the most sensitive diagnostic test in these infants.
  - Collect serum specimen from infant (cord blood at birth is good), and send to the SLI for rubella IgM testing. If positive for rubella IgM, fetal infection has occurred. Ninety to 97% of CRS infants aged 2 weeks to 3 months have IgM, but only 80% of CRS babies are IgM positive by some laboratory tests, so a negative rubella IgM result by itself does not rule out the possibility of infection. Retesting is indicated if there is a high index of suspicion.
  - If infant is negative for rubella IgM at birth, collect another serum at age $\geq$3 months and another specimen 1 month later, and send to the SLI (with the specimen collected at birth, if available) for paired testing for rubella IgG. If only passive transfer of maternal IgG antibody has occurred, the baby's titer would be expected to drop at a rate of a two-fold dilution per month. If fetal infection has occurred, the titer will persist and not drop as quickly.

Pending laboratory confirmation (or rule-out), notify the pediatrician of the need for long-term follow-up. Confirm the CRS or congenital rubella infection only diagnosis with laboratory testing (see *Attachment B: Instructions for*

* Limited data indicate that IG in a dose of 0.55 mL/kg may prevent or modify infection in an exposed, susceptible person. In one study, the attack rate of clinically apparent infection was reduced from 87% in control subjects to 18% in recipients of IG. However, the absence of clinical signs in a woman who has received IG does not guarantee that fetal infection has been prevented. In this study, 44% of the IG recipients were infected. Infants with congenital rubella are known to have been born to mothers who were given IG shortly after exposure.

Collection of Serologic Specimens from Suspect Cases [Including CRS Infants]). Report all CRS and congenital rubella infection only cases to the MDPH as soon as they are suspect, even though laboratory confirmation might be pending. Cases are reported to the federal Centers for Disease Control and Prevention (CDC) and are then entered into the National Congenital Rubella Syndrome Registry.

The following data are important and should be collected during case investigation (additional information will also need to be collected):

- Demographic information.
- Maternal history, including: a) date of rubella vaccination(s); b) dates and results of previous serologic tests for rubella immunity; c) history or documentation of rubella infection during pregnancy; d) history of pregnancies inside and outside the U.S.; e) country of birth and length of residence in the U.S.; and f) history of exposure to rubella and travel.
- Clinical details (e.g., cataracts, hearing impairment, developmental delay, type of congenital heart defect, meningoencephalitis, microcephaly).
- Laboratory information, including types and results of laboratory testing performed on both mother and child.

As mentioned above, instances of deafness have been documented even when maternal infection occurs after 20 weeks gestation.

3. Rubella Prevention and Control

Recommend that pregnant women with unknown immune status restrict activities to avoid exposure while waiting for serologic test results. During this time, pregnant women should be excluded from activities (e.g., work or school) that present the possibility of exposure to persons with confirmed or suspect cases of rubella. Pregnant women found to be susceptible to rubella should avoid these settings for six weeks (two incubation periods) after the onset of symptoms of rubella in the last patient for whom rubella cannot be ruled out.

During outbreaks, susceptible pregnant women should be advised to avoid the affected setting(s) (e.g., schools, military settings, workplace, churches, athletic events, or other social gatherings).

Remember to evaluate all adults, especially women of childbearing age (12–50 years of age), for needed immunizations at every encounter with the health care system. All foreign-born adults without vaccination records should be vaccinated with MMR.

It is important to vaccinate all susceptible post-partum women prior to discharge from the hospital.

Note: Previous administration of human anti-Rho(D) immune globulin (RhoGam) does not generally interfere with an immune response to rubella vaccine. However, women who have received anti-Rho immune globulin should be serologically tested 6–8 weeks after vaccination to assure that seroconversion occurred. If other antibody-containing blood products are needed for other reasons, they should be administered at least 2 weeks before and deferred for up to 11 months after administration of MMR vaccine.

State-supplied MMR vaccine is available for use in the following groups and sites:

Availability of State-Supplied MMR Vaccine

- All children through 18 years of age in both public and private clinics.
- Post-partum women at all maternity hospitals state-wide.
- High-risk adults seen in the public sector.

The Massachusetts Immunization Program (MIP) will provide detailed rubella infection control recommendations. Please call a MDPH immunization epidemiologist at (617) 983-6800 or (888) 658-2850.

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Attachment B

Instructions for Collection of Serologic Specimens from Suspect Cases (Including CRS Infants)

SLI Virology Laboratory—Room 815
305 South Street
Boston, MA 02130

Note: Specimens must be submitted with a completed SLI Specimen Submission Form (found at the end of this chapter and on the MDPH website at www.mass.gov/dph/bls/generalform.pdf).

Antibody Detection

Submission of specimens to the SLI Virology Laboratory must be coordinated through a MDPH immunization epidemiologist at (617) 983-6800 or (888) 658-2850. Technical questions about specimen collection can be addressed to the SLI Virology Laboratory at (617) 983-6383 or (617) 983-6396.

Specimen Type	Serum for IgM Antibody (Serology for Acute Infection)
Collection Procedure	Venipuncture. Serum-separator tubes (SST) preferred, red-top tubes acceptable.
Optimum Collection Time	CRS: At birth or as soon as possible after birth. Exposed pregnant women: Immediately. Rubella (non-CRS): ≥3 days after rash onset. Note: In all of the above cases, follow-up specimens for additional testing may be required.
Transportation Container	Serum in polystyrene (plastic) tube, or blood in SST, preferably centrifuged.
Volume	2 mL serum; ≥0.5 mL may be acceptable for young children.
Transport	Cold, use ice packs. **DO NOT FREEZE**.

Serum for IgG antibody testing is performed at the SLI under special circumstances, after consultation with a MDPH immunization epidemiologist. If approved, follow same procedures described above.

Viral Isolation

Specimen Collection for Isolation of Rubella Virus from Cases of CRS or Acute Rubella

In addition to serum specimens for the serological diagnosis of rubella, clinical specimens for viral isolation are helpful to confirm a positive serum result and for viral surveillance of rubella genotypes. The instructions on the next page provide guidance on specimen collection for suspect cases of rubella and CRS. Throat swabs are the preferred clinical specimen for viral isolation in suspect cases of rubella. However, nasopharyngeal (NP) swabs may be easier to obtain in infants with suspect CRS. Urine should be collected but virus recovery is lower from this clinical specimen.

Submission of specimens must be coordinated with a MDPH immunization epidemiologist, at (617) 983-6800 or (888) 658-2850, who can facilitate the shipment of specimens to the SLI in a timely manner.

Updated 3/2005

Specimen Collection for Isolation of Rubella

	Throat Swab/Oropharyngeal Swab (This is the preferred sample for rubella virus.)	**Nasopharyngeal (NP) Swab** (This is an alternative for infants with CRS in whom oropharyngeal specimens may not be possible. A NP swab may be pooled with a throat swab to ensure an adequate sample.)	**Urine** (Throat or NP specimens have higher rates of rubella virus recovery than urine.)
Collection Procedure	Use a cotton/dacron swab to collect the specimen. Swab the posterior pharynx and tonsillar areas, avoiding the tongue (tongue depressor may be helpful). The mucosa behind the uvula and between the tonsils should be gently swabbed with a back-and-forth motion.	Use a cotton/dacron swab to collect the specimen. Insert sterile swab into nasopharynx, rotate, and remove. Alternative method is a nasal wash/aspirate using a syringe attached to a small, plastic tube and 3–5 mL of Viral Transport Media (VTM). After placing VTM in nose, aspirate as much of the material as possible.	Collect clean void, first morning if possible.
Optimum Collection Time	Optimal collection for virus isolation is within the first three days of rash onset. After five days, the recovery of virus is much lower in the case of acute rubella. For CRS, collect samples at birth or as soon as possible after birth. Virus can often be cultured from cases of CRS up to three months after birth.	As for throat swabs.	As for throat swabs.
Transportation Container	Place swab in Viral Transport Media (VTM). Any sterile isotonic fluid, like phosphate buffered saline (PBS) or common tissue medium like Eagle's MEM, can be used. Commercially available kits containing swabs and VTM are acceptable (e.g., BECTON DICKINSON). Swabs may be broken off and shipped with media. Keeping swabs moist is most important. Alternatively, swirl/agitate the swab in the media for several minutes before removal.	Place swab in Viral Transport Media (VTM). Any sterile isotonic fluid, like phosphate buffered saline (PBS) or common tissue medium like Eagle's MEM, can be used. Commercially available kits containing swabs and VTM are acceptable (e.g., BECTON DICKINSON). Swabs may be broken off and shipped with media. Keeping swabs moist is most important. Alternatively, swirl/agitate the swab in the media for several minutes before removal. Aspirate should be placed in a leak-proof plastic tube.	Sterile plastic, leak-proof container.
Volume	3–5 mL of VTM	3–5 mL of VTM	10 mL
Transport	Cold, on ice packs. Should be received at the laboratory within 48 hours of collection. If shipment is delayed and facilities are available, the specimens should be frozen at -70°C and shipped on dry ice. Otherwise, store specimens in refrigerator (freezing at -20°C reduces viability of virus).	As for oropharyngeal specimens.	Cold, on ice packs.

Coordinate specimen submission with the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

Attachment C

Measles, Mumps, Rubella (MMR) Vaccine Fact Sheet

The following should be considered when administering measles, mumps, rubella (MMR) vaccine or vaccines that contain one or more MMR component:

A. Allergy to Eggs

Hypersensitivity to eggs is not a contraindication per the American Academy of Pediatrics (AAP) and Advisory Committee on Immunization Practices (ACIP). Most allergic reactions following administration of MMR have been attributed to trace amounts of gelatin, neomycin, or other vaccine component (see below). Recent data have demonstrated the safety of MMR vaccine, even in those with a history of egg anaphylaxis. Skin testing is not predictive and not recommended in persons with a history of egg allergy.

Recommendations

Routinely vaccinate, as indicated, those with an egg allergy with any of these vaccines:

- Monovalent measles vaccine,
- Monovalent mumps vaccine,
- Monovalent rubella vaccine (rubella vaccine is not grown in chicken embryo cell culture), or
- MMR vaccine.

B. Allergic Reactions to Neomycin and Gelatin

Neomycin allergy most often manifests as a contact dermatitis. Non-anaphylactic reactions to either neomycin or gelatin are NOT contraindications to MMR vaccine.

Recommendations

Persons who have experienced true anaphylactic reactions to topically or systemically administered neomycin or to gelatin should receive MMR vaccine only in settings where such reactions can be managed and after consultation with an allergist or immunologist.

C. MMR Vaccine and Autism, Associated Disorders, and Inflammatory Bowel Disease

The Institutes of Medicine (IOM) Immunization Safety Review Committee has concluded that the recent increases in autism and related disorders are not attributable to MMR vaccine. The AAP convened a panel of experts that also found that the available evidence does not support the hypothesis that MMR vaccine causes autism, associated disorders, or inflammatory bowel disease.

Recommendations

Follow existing recommendations for routine use of MMR vaccine at 12–15 months of age and a 2nd dose at 4–6 years of age.

D. Acute Arthritis/Arthralgia

Arthralgia (joint pain) and arthritis can occur in susceptible individuals post-vaccination with MMR. Joint pain has been reported in 0.5% of children. Up to 25% of post-pubertal females may develop arthralgia, and up to 10% may develop transient arthritis. If joint symptoms occur post-vaccination, they generally begin 1–3 weeks post-vaccination, are transient, and last only 1–21 days. Symptoms of acute arthritis/arthralgia are much less common post-vaccination than with natural disease.

Recommendations

Vaccinate susceptible women of childbearing age because the potential risks of a susceptible woman having a child with congenital rubella syndrome (CRS) far outweigh risks of adverse events related to joint abnormalities.

E. Thrombocytopenia Purpura

MMR can rarely cause clinically apparent thrombocytopenia within 2 months of vaccinations, with temporal clustering 2–3 weeks after vaccination. Reported cases have been transient and benign in outcome. The estimated number of cases is 2 per 1 million doses distributed in the U.S. However, based on these case reports, the risk of vaccine-associated thrombocytopenia may be higher for those who have had a previous episode of thrombocytopenia, especially if it occurred in temporal association with earlier MMR vaccination.

Recommendations

If an individual has a prior history of thrombocytopenia:

- Check for serologic immunity (if immune, vaccination is NOT indicated), and
- Assess risk/benefit of vaccination.

In most cases, the benefits of vaccination will justify giving the vaccine.

F. Altered Immune Status

Enhanced replication of vaccine viruses may occur in persons who have immune deficiency disorders and are immunocompromised. For some of these conditions, all affected persons are severely immunocompromised. The degree to which the immune system is compromised depends on the severity of the condition, which in turn depends on the disease or treatment stage. The patient's health care provider must assume responsibility for determining whether the patient is severely immunocompromised based on clinical and laboratory assessment.

Recommendations

- Do not administer MMR vaccine to patients who are severely immunocompromised for any reason.
- Administer MMR vaccine to healthy susceptible contacts of severely immunocompromised persons.

G. MMR Vaccine for HIV-Infected Individuals

Because measles can be severe and often fatal in patients with HIV infection, MMR vaccine is recommended for people with asymptomatic HIV infection who are not severely immunocompromised. Severely immunocompromised HIV-infected patients, as defined by low CD4+ T-lymphocyte counts (considering age), should not receive measles virus-containing vaccine because vaccine-related pneumonia has been reported.

Recommendations

- Routine pre-vaccination HIV testing is NOT recommended.
- Administer MMR vaccine for routine immunization of individuals with asymptomatic HIV infection who do not have evidence of severe immunosuppression.
- Consider MMR vaccine for all symptomatic HIV-infected persons who do not have evidence of severe immunosuppression, as defined in the table below.

Measles-containing vaccines are contraindicated in those with the following:

Age Group	Total CD4+ Count	or	CD4+ as a % of Total Lymphocytes
<12 months	<750/mcL	or	<15%
1–5 years	<500/mcL	or	<15%
6–12 years	<200/mcL	or	<15%
≥13 years	<200/mcL	or	<14%

Source: CDC. Measles, Mumps and Rubella—Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome, and Control of Mumps: Recommendations of the ACIP. *MMWR*. 1998; 47(RR-8): 21.

- Do not administer MMR or other measles-containing vaccines to severely immunocompromised HIV-infected individuals (as defined by low CD4+ counts or low percent of CD4+ circulating lymphocytes—see above table).
- Since the immunologic response to vaccines is often poor in HIV-infected patients, give the 1st dose of MMR as early as possible after 12 months of age. This will increase the chance of an adequate immune response, before further deterioration of the immune system can occur.
- Give the second dose of MMR four weeks after the first. This will increase the likelihood of seroconversion.
- During outbreak situations only, consider giving the first dose of monovalent measles vaccine (or MMR if monovalent measles vaccine is not available) at 6–11 months of age to those infants who are not severely immunocompromised. Remember, these children must be revaccinated with 2 doses of MMR beginning at 12 months of age. If possible, avoid giving mumps and rubella at <12 months of age.
- Administer MMR vaccine to health contacts of severely immunocompromised persons.

H. Live Virus Vaccines and Immunosuppressive Therapy

Recommendations

- After chemotherapy and other immunosuppressive therapy (except steroids—see table on the next page), defer MMR vaccine for ≥3 months.
- For patients on steroids, defer live virus vaccines as outlined in the table on the next page.

Guidelines for Administration of Live Virus Vaccines and Steroid Therapy *

Steroid Therapy	Recommendations for Deferral
High dose systemic steroids daily or on alternate days for ≥14 days (≥2mg/kg QD or ≥20mg QD of prednisone)	Defer live virus vaccines for ≥1 month after treatment has stopped.
High dose systemic steroids daily or on alternate days for <14 days (≥2 mg/kg QD or ≥20 mg QD prednisone)	Can give live virus vaccines immediately after treatment is discontinued. However, some experts recommend deferring until two weeks after treatment has stopped, if possible.
Low or moderate doses of systemic steroids given daily or on alternate days (<2 mg/kg QD or <20 mg QD of prednisone); or physiologic maintenance doses of steroid (replacement therapy)	Can give live virus vaccines on treatment.
Topical, aerosol, or local injections of steroids (e.g., skin, aerosol, eyes, intra-articular, bursal, tendon injections)	Can give live virus vaccines on treatment. However, if this therapy is prolonged and there is any clinical or laboratory evidence of immunosuppression, defer for ≥1 month after treatment has stopped.
Individuals with a disease which in itself is considered to suppress the immune response and who are receiving systemic or locally acting steroids	Should not give live virus vaccines, except in special circumstances.

Adapted from : American Academy of Pediatrics. [Immunization in Special Clinical Circumstances.] In: Pickering L.K., ed. *Red Book: 2003 Report of the Committee on Infectious Diseases, 26th Edition*. 2003: 74–75.

* Steroid therapy is not a contraindication for administration of killed vaccines.

I. MMR Vaccine and Pregnant Women

MMR vaccine is contraindicated in pregnant women due to the theoretical risk to the fetus. To date, there are no data demonstrating any ill effects on developing fetuses. Current data, estimated risk, and recommendations are outlined below.

Rubella

There is no evidence that rubella vaccine causes CRS. However, pregnant women should not be immunized due to the theoretical risk to the fetus, estimated to be potentially, on a statistical basis, 0–1.6%, based on data accumulated by the CDC on 226 susceptible women who received the current RA27/3 vaccine strain during the first trimester. Only 2% of the babies had asymptomatic infection but none had congenital defects. This risk is substantially less than the ≥20% risk for CRS associated with maternal infection in the first trimester of pregnancy. In view of these observations, receipt of rubella vaccine in pregnancy is not an indication for termination of pregnancy.

Mumps

There is no evidence that mumps vaccine will cause mumps infection in an unborn fetus. Live mumps vaccine can infect the placenta, but the virus has not been isolated from fetal tissue.

Measles

There is no evidence that measles vaccine will cause measles infection in an unborn fetus.

Recommendations

- Screening: Ask women of childbearing age if they are pregnant. Routine pre-vaccination pregnancy testing is NOT recommended. The American College of Obstetricians and Gynecologists (ACOG), the ACIP, and the AAP all state that it is sufficient to screen by asking a woman if she is pregnant.
- Patient advice: Inform women of the theoretical risk to the fetus if they are pregnant or plan to become pregnant within four weeks following vaccination. In view of this theoretical risk, advise them not to become pregnant for four weeks following MMR vaccine.
- Vaccination: Do not vaccinate women who are pregnant.
- Documentation: Date of last menstrual period (LMP) and the advice given to the patient may be documented in the woman's chart.

J. MMR and Tuberculosis (TB) Testing

Measles vaccination may temporarily suppress tuberculin skin test reactivity.

Recommendation

If TB testing cannot be done the day of MMR vaccination, postpone the test for 4–6 weeks.

K. Invalid Doses

Consider doses of measles, mumps, or rubella vaccines invalid in the following situations:

- Received before first birthday.
- Received after recent receipt of IG (please refer to *Attachment D: Use of Immune Globulin [IG]* of the measles chapter).
- Killed measles vaccine.
- Killed measles vaccine followed by live vaccine within three months (both doses are invalid).
- Measles vaccine of unknown type received prior to 1963–1967.
- Simultaneous receipt of IG and either a further attenuated measles vaccine (i.e., containing Schwartz or Moraten strains) or measles vaccine of unknown type.
- Killed mumps vaccine.
- Mumps vaccine of unknown type received prior to 1979.
- Live rubella vaccine accompanied by IG.

Re-vaccination with MMR is recommended for eligible individuals such that at least two valid doses of measles-containing vaccine, one of mumps and one of rubella, are documented.

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FORMS & WORKSHEETS

Rubella

(Also known as German Measles)

Rubella

REPORT IMMEDIATELY

(Also known as German Measles)

LBOH Action Steps

This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to rubella case investigation activities.

LBOH staff should follow these steps when rubella or congenital rubella syndrome (CRS) is suspected or confirmed in the community. For more detailed information, including disease epidemiology, reporting, case investigation, and follow-up, refer to the preceding chapter.

Note: Due to the health implications of rubella and CRS, as well as national surveillance and reporting requirements, the MDPH epidemiologists will usually take the lead on rubella and CRS investigations. This includes filling out the official case report form and making case management recommendations, in collaboration with the LBOH. MDPH epidemiologists will keep the LBOH informed of all significant developments and will request the assistance of the LBOH as needed.

Reporting

- ❑ Immediately notify the MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, to report any confirmed or suspect case(s) of rubella.

Case Investigation

- ❑ Work with MDPH to ensure that appropriate clinical specimens are collected and submitted to the SLI for confirmation.
- ❑ Work with MDPH to obtain the information necessary for completion of the case report form, including source of exposure, clinical information, vaccination history, laboratory results, and source of infection (MDPH will complete the form and submit to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services [ISIS]).

Prevention and Control

- ❑ Work with MDPH to institute isolation and quarantine requirements *(105 CMR 300.200)* and other control measures, as they apply to a particular case.
- ❑ Identify high-risk (e.g., pregnant women) and susceptible individuals, including those with medical or religious exemptions.
- ❑ Vaccinate susceptible individuals with rubella-containing vaccine (if not contraindicated). MMR vaccine is preferred.
- ❑ Conduct surveillance for two incubation periods.

Managing Rubella in Schools and Other Institutions

In addition to the prevention and control measures described above:

- ❑ Notify and educate staff, students, and/or patients.
- ❑ Test and exclude symptomatic individuals.
- ❑ Isolate remaining susceptible contacts as indicated. (But in many non-health care settings, susceptibles may be readmitted if they receive post-exposure vaccination.)

Managing Rubella in Health Care Settings

In addition to the prevention and control measures described above:

- ❑ Notify infection control or employee health of confirmed or suspect case(s) in institution.
- ❑ Ensure all health care personnel have proof of immunity appropriate for health care setting.
- ❑ Use more rigorous criteria for exclusion/isolation for susceptibles in health care setting as described in the chapter.
- ❑ In health care setting, susceptibles who get vaccinated after exposure are not allowed to return to work until after the exclusion period.